

## REMARKS / ARGUMENTS

In response to the office action of October 8, 2008, Applicants have amended the claims, which when considered with the following remarks, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is respectfully requested.

Claims 15, 16 and 18 have been objected to for various informalities as set forth on page 2 of the office action. In response thereto, claim 15 has been amended to recite "consisting of" rather than "consisting in." The misspelling in claim 15 has also been corrected and "pro cm<sup>2</sup>" in claims 16 and 18 has been corrected to "per cm<sup>2</sup>." Accordingly, withdrawal of the objections to claims 15, 16 and 18 is respectfully requested.

The abstract of the disclosure has been objected to due to the alleged use of legal phraseology such as "comprising", "said" and "wherein." By this amendment, a replacement abstract is submitted on a separate sheet. The replacement abstract no longer uses the terms "comprising", "said" and "wherein." Withdrawal of the objection to the abstract is therefore warranted.

Claims 1-19 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, it is the position of the Examiner that it is not clear whether the terms in parentheses in claim 1 are intended to further limit the subject matter of the claim or just to provide alternative terminology. By this amendment, claim 1 no longer recites "(internal)" and "(external)". Withdrawal of the rejection of claims 1-19 under 35 U.S.C. 112, second paragraph, is therefore respectfully requested.

Claims 1-19 have been rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Tanizawa et al. (US 2004/0018235) and Dittmar et al. (U.S. 6,893,662) in view of Dansereau et al. (US 5,032,406).

Applicants respectfully traverse the rejection for the following reasons. The present invention requires a specific structure of the pharmaceutical composition for sustained release, which is in particular characterized by a specific order of the various coatings or phases. Namely, the pharmaceutical composition as claimed in the present application has a core which is a two-phase core, comprising an inner or internal phase and an outer or external phase, meaning that the internal or inner phase is covered by or coated with the outer or external phase. Furthermore, it is important to emphasize that the outer or external phase does not comprise a matrix former. This two-phase core element of the pharmaceutical composition of the present invention is first coated with a non-functional film coat and subsequently with an enteric coat, so that the enteric coat is the outermost layer of the layers as defined in independent claim 1.

In accordance with the teachings of the present application, this specific structure enables the provision of a highly stable composition for pitavastatin enabling a desired, sustained and slow release, which can be easily manufactured and which has also beneficial effects with respect to pharmacological properties, namely increased distribution of the active principle to the liver in combination with a slow release leading to reduced drug plasma levels which in turn are responsible for better tolerability as well as less side effects, when compared with other types of pharmaceutical compositions for the active principle of relevance for the present invention.

Tanizawa et al. neither hints at or suggests a structure of a pharmaceutical composition as defined in the present invention. The structure of the pharmaceutical composition of the present invention is completely contrary to the teachings of Tanizawa et al. Tanizawa et al. discloses a pharmaceutical composition which can be regarded as a two-phase composition, which comprises as innermost layer or particle an enteric composition, which is then in any case (i.e. independent from the fact whether or not the pharmaceutical composition of Tanizawa is formed as a dual layer composition or a core shell composition) always coated with a non-enteric composition. This non-enteric composition comprises active principle which is to be released early, as well as a matrix former, needed for the formation of a coating layer in accordance with the description of Tanizawa.

In contrast, the present invention provides an enteric coating on the outside which is not required to contain the pharmaceutically active ingredient, since the active principle is contained in the core of the pharmaceutical composition, i.e. in the two-phase core comprising the internal and external phase.

In addition, Tanizawa et al. emphasizes that it is important for the technical teaching as disclosed therein that a certain amount of the active principle is already released in the stomach. In contrast, the present invention aims at completely preventing the release of the active principle already in the stomach, namely by means of the enteric coating provided as the outermost layer, as recited in claim 1.

Accordingly, no skilled person would ever contemplate a modification of the pharmaceutical composition as disclosed in Tanizawa et al. being a modification leading to the pharmaceutical composition of the present invention, since the present invention is concerned with a technical teaching clearly not considered as advisable by the technical teaching of Tanizawa et al.

Concerning the references to the examples of Tanizawa et al. as made by the Examiner on page 6 of the Office Action, it has to be emphasized again that it is irrelevant whether or not Tanizawa discloses a pharmaceutical composition which may be considered as a pharmaceutical composition with a core of two layers, one outer and one inner layer. All the examples of Tanizawa require that the outer layer is made from the non-enteric coating, which furthermore comprises a matrix former, so that when compared with the core of the pharmaceutical composition of the present invention a further difference is readily apparent, namely the presence of a matrix former in the pharmaceutical composition of Tanizawa, whereas the present invention requires, for the outer phase of the core, the absence of such a matrix former.


Dittmar et al. is only concerned with the provision of specific outer coatings on pharmaceutical compositions without, however, specifically pointing out that the coating layers should be as defined in the present invention and, in particular, should be implied to a two-phase core structure as defined in the present invention. In this context, it is furthermore entirely clear that no skilled person would consider combining the disclosure of an enteric coating as outer coating (Dittmar et al. ) with the disclosure of the pharmaceutical

composition of Tanizawa. The enteric coating of Dittmar et al. on top of the pharmaceutical composition of Tanizawa would make absolutely no technical sense in view of the fact that Tanizawa, in fact, teaches that the pharmaceutical composition is not coated on the outside with an enteric coating since such enteric coating would prevent the desired liberation of a part of the active principle already in the stomach. Therefore, no skilled person would combine Tanizawa et al. with Dittmar et al. in the first instance.

Dansereau et al. does not cure the deficiency of teachings provided by Tanizawa et al. and Dittmar et al. Dansereau et al. requires the presence of a polymer matrix, i.e. a matrix former. In contrast, the outer or external phase of the core of the pharmaceutical composition of the present invention requires the complete opposite, namely the absence of a matrix. Accordingly, even if, *a priori*, one skilled in the art would have combined the references in the manner the Examiner has done, the skilled artisan would still not have arrived at the present invention. Withdrawal of the rejection of claims 1-19 under 35 U.S.C. § 103(a) is therefore respectfully requested.

In view of the amendments to the claims, and the foregoing remarks, the present application is believed to be in condition for allowance, which action is earnestly solicited.

Respectfully submitted,

  
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